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Date: September 27, 2005 **Total pages:** 12 w/cover sheet

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Our Docket No. YU 182
Your Docket No. **Client/Matter No: 078245-00045**

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MESSAGE:
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Peter M. Glazer

Serial No: 09/978,333 Art Unit: 1634

Filed: October 15, 2001 Examiner: Carla Myers

For: *TRIPLE-HELIX FORMING OLIGONUCLEOTIDES FOR TARGETED MUTAGENESIS*

Attachments:
Transmittal Form PTO/SB/21;
Fee Transmittal PTO/SB/17;
Submission of Decision on Appeal; and
Decision on Appeal

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PTO/SB/21 (09-04)
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	09/978,333
Filing Date	October 15, 2001
First Named Inventor	Peter M. Glazer
Art Unit	1634
Examiner Name	Carla Myers
Attorney Docket Number	YU 132

ENCLOSURES *(Check all that apply)*

- [✓] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation
- [ ] Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- [ ] Proprietary Information
- [ ] Status Letter
- [✓] Other Enclosure(s) (please identify below):
  Decision on Appeal

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Pabst Patent Group LLP		
Signature			
Printed name	Patrea L. Pabst		
Date	September 27, 2005	Reg. No.	31,284

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Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL For FY 2005

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 0.00

Complete if Known	
Application Number	09/978,333
Filing Date	October 15, 2001
First Named Inventor	Peter M. Glazer
Examiner Name	Carla Myers
Art Unit	1634
Attorney Docket No.	YU 132

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FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES Fee ($)	FILING FEES Small Entity Fee ($)	SEARCH FEES Fee ($)	SEARCH FEES Small Entity Fee ($)	EXAMINATION FEES Fee ($)	EXAMINATION FEES Small Entity Fee ($)	Fees Paid ($)
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple dependent claims	360	180

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)	Multiple Dependent Claims Fee ($)	Multiple Dependent Claims Fee Paid ($)
17 - 20 or HP =	_____ x	0.00	= 0.00	_____	_____

HP = highest number of total claims paid for, if greater than 20

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
1 - 3 or HP =	0 x	0.00	= 0.00

HP = highest number of independent claims paid for, if greater than 3

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
_____ - 100 =	_____ / 50 =	_____ (round up to a whole number)	x _____	= _____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English Specification, $130 fee (no small entity discount)	
Other: _____	

SUBMITTED BY

Signature		Registration No. (Attorney/Agent) 31,284	Telephone (404) 879-2151
Name (Print/Type)	Patrea L. Pabst		Date September 27, 2005

This collection of information is required by 37 CFR 1.138. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Peter M. Glazer		
Serial No.:	09/978,333	Art Unit:	1634
Filed:	October 15, 2001	Examiner:	Carla Myers

For: *TRIPLE-HELIX FORMING OLIGONUCLEOTIDES FOR TARGETED MUTAGENESIS*

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SUBMISSION OF DECISION ON APPEAL IN U.S.S.N. 09/783,338

Sir:

Further to the Appeal Brief filed September 21, 2005, Appellant submits a copy of the Decision of Appeal in U.S.S.N. 09/783,338 reversing the Examiner's rejection of the claims for lack of enablement under 35 U.S.C. § 112, first paragraph, for consideration by the Examiner of the above-referenced application. Appellant noted in the Appeal Brief filed September 21, 2005 that the appeal in U.S.S.N. 09/783,338 addresses similar issues addressed in the Appeal Brief of the above-referenced application.

U.S.S.N.: 09/978,333
Filed: October 15, 2001

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Respectfully submitted,

Patrea L. Pabst
Reg. No. 31,284

Date: September 27, 2005

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte PETER M. GLAZER and PAMELA A. HAVRE

Appeal No. 2005-0733
Application No. 09/783,338[1]

HEARD: July 14, 2005

Before SCHEINER, ADAMS and MILLS, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 6-14 (the only claims remaining in the application) under the first paragraph of 35 U.S.C. § 112. There is no dispute that "the central issue on Appeal is whether the claims, as they relate to [an] in vivo [method], lack enablement." Reply Brief, page 1.

The present application is a continuation of U.S.S.N. 08/083,088.[2] The claims in the parent application were much the same as the claims in the present application (see the comparison below), and were rejected on the same basis. Following an appeal of the rejection in that case (Appeal No. 1997-2520, opinion dated February 28, 2001), the board agreed that the examiner had established a reasonable basis for questioning the enablement of the claims, and affirmed the examiner's rejection.

[1] Application for patent filed February 14, 2001.

According to appellants, "[e]vidence showing in vivo as well as additional evidence of in vitro efficacy was obtained after filing of the appeal [in the parent case], but could not be considered in [that] appeal. The present application was filed so that such evidence could be considered (submitted in the form of a Declaration under [37 CFR § 1.132])." Brief, page 2.

THE CLAIMED SUBJECT MATTER

Claim 6 is representative of the subject matter on appeal and reads as follows:

6. A method for site-directed mutagenesis of a nucleic-acid molecule comprising the steps of:

a) hybridizing a mutagenic oligonucleotide to a target region of a double-stranded nucleic acid molecule, wherein the mutagenic oligonucleotide comprises a mutagen incorporated into a single-stranded nucleic acid that forms a triple-stranded nucleic acid molecule with the target region; and

b) mutating the double-stranded nucleic acid molecule.

The corresponding claim in U.S.S.N. 08/083,088 is as follows (differences emphasized):

6. A method for site-directed mutagenesis of a nucleic acid molecule **consisting of** steps of:

a) hybridizing a mutagenic oligonucleotide to a target region of a double-stranded nucleic acid molecule **in a cell**, wherein the mutagenic oligonucleotide comprises a mutagen incorporated into a single-stranded nucleic acid that forms a triple-stranded nucleic acid molecule with the target region; and

b) mutating the double-stranded nucleic acid molecule.

DISCUSSION

In deciding the appeal in U.S.S.N. 08/083,088 (Appeal No. 1997-2520), the parent of the present application, the board considered the examiner's thorough analysis of appellants' disclosure under the so-called Wands factors,[3] and concluded that "the totality of the evidence presented by the examiner and appellants weigh[ed] in favor of finding lack of enablement of the claimed invention" (page 13 of the opinion in Appeal No. 1997-2520). In the present case, however, appellants have submitted "[e]vidence of reduction to practice in intact animals . . . in the form of a Declaration . . . to prove the truth of the statements in the application" (Brief, page 7). As the examiner explains, "the Declaration by Dr. Glazer[4] . . . represents the only new evidence in this application" (Answer, page 10), so we will focus our discussion on whether or not the Declaration is adequate to address the examiner's concerns and to rebut the examiner's rejection.

In a nutshell, the examiner's concerns with respect to the in vivo aspects of the claimed invention involve "issues of [oligonucleotide] delivery, penetration," and "triplex formation" (Answer, page 7) in an intact animal. The examiner acknowledges that "[t]he specification [demonstrates] site specific, targeted mutagenesis . . . in an in vitro method" and "in an ex vivo type method" (id., page 5), but argues that "there is no

---

[3] Factors to be considered in determining whether a disclosure is unenabling because it would require undue experimentation to practice the invention have been summarized by the board in Ex parte Forman [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims (footnote omitted).

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

[4] Submitted December 3, 2002.

correlation between the entry of the oligonucleotide-mutagen complex in isolated cells in an ex vivo method and in vivo applications where entry into an animal is required" (id.), largely because "the precise role of nucleases, other intracellular enzymes and proteins on the stability of [ ] ribozymes, . . . [mechanisms] by which oligonucleotides penetrate cellular membranes and distribute in cells, [ ] non-sequence-specific interactions[,] . . . metabolism of antisense drugs . . . and cellular parameters such as cell type, cell cycle phase and differentiation stage" (id., page 6) are poorly understood and unpredictable.

In his declaration, Dr. Glazer describes the protocols and results of experiments in which mice were given intraperitoneal injections of a triplex-forming oligonucleotide (TFO) designed to bind to a predetermined site on the *supFG1* gene. See section 12, pages 6-14 of the Declaration. The examiner does not dispute Dr. Glazer's assertion that the mouse experiments described in the Declaration "demonstrate that site-specific, TFO-directed genome modification can be accomplished in intact animals" (Declaration, page 7). Rather, the examiner argues that the in vivo experiments described in the Declaration are not commensurate in scope with the claimed invention because the mutagenic oligonucleotide used in the mouse experiments differs from the oligonucleotide used in the specification's in vitro and ex vivo examples in that it does not have a discrete mutagen associated with it. See pages 11 and 12 of the Answer.

As explained by Dr. Glazer, however, in vitro experiments established that targeted mutagenesis was seen with and without psoralen[5] conjugation, "suggesting a substantial triplex-mediated process of mutagenesis" (Declaration, page 7), and appellants argue that "there has been no evidence provided by the examiner that the

[5] Psoralen is a known mutagen.

in vivo evidence in the Declaration would not be predictive of an oligonucleotide which further included a small molecule mutagen such as a psoralen" (Reply Brief, page 5). In any case, it does not appear that the examiner has questioned the ability of an attached mutagen to cause a mutation in a double-stranded nucleic acid molecule, once delivered to a cell.

In our opinion, the examiner has not explained why the mouse experiments described by Dr. Glazer are not relevant to the examiner's stated concerns: "issues of [oligonucleotide] delivery, penetration," and "triplex formation" (Answer, page 7). On this record we see no reason to dispute appellants' assertion that the experiments described in the Declaration demonstrate "the ability of the oligonucleotide to specifically bind the target gene[;] formation of a stable complex between the oligonucleotide and the target gene[;] uptake of the oligonucleotide by the cell[;] and [ ] solubility of the nucleotide in the cell" (Brief, page 12).

Finally, we note the examiner's assertion that "simply correcting a few cells of [an] arbitrary mutation created in the mouse is not enough for a patentable use" "since no therapeutic effect has been shown for any of the oligonucleotides" (Answer, page 11) and in any case, "[t]he mutations must be corrected in sufficient amounts to yield some benefit or there is no patentable use for the correction method" (Id., pages 11-12). Nevertheless, the claims have not been rejected as lacking utility, and we perceive no requirement in the claims that the method have any therapeutic effect.

In our view, the Declaration of Dr. Glazer provides evidence sufficient to rebut the examiner's initial basis for questioning the enablement of the claimed invention. Accordingly, the rejection of claims 6-14 under the first paragraph of 35 U.S.C. § 112 is reversed.

REVERSED

Toni R. Scheiner
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES

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